REMARKS

Objection to Specification

In response to the "Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures," Applicants submit herewith an initial paper copy of a Sequence Listing in accordance with 37 C.F.R. § 1.821(c), which corresponds to the sequence disclosure on page 26, lines 5-6, of the specification.

In addition, Applicants submit herewith a 3.5" diskette containing a computer readable form of the Sequence Listing, which corresponds to the sequence disclosure on page 26, lines 5-6, of the specification.

As required under 37 C.F.R. § 1.821 (f) and (g), Applicants hereby state that the sequence listing information recorded in computer readable form is identical to the written (i.e., paper copy) sequence listing, and that no new matter has been added.

In view of the preceding, Applicants respectfully submit that the present application is in full compliance with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures. Accordingly, withdrawal of this ground of objection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112, First Paragraph – Written Description

The written description rejection of claims 72-77, 80-81, 83-88, 100-101, and 103-106 under 35 U.S.C. § 112, first paragraph is respectfully traversed. The recitations in the claims of terminology such as "hapten," "marker group," "solid phase binding group," "reactive side groups," "predetermined positions," and "non-immunologically reactive" would be clear to one of ordinary skill in the art based on both the description in the specification and the well-established definitions of these terms.

For example, it is well understood in the art that the term "hapten" refers to a portion of an immunogen. A discussion of the term "hapten" excerpted from *Applications of Fluorescence in Immunoassays* by I. A. Hemmilä (Chapter 2.1.1, pp. 4-7; Tables 8.9-8.12, pages 188-193) is attached herewith as Exhibit A. Moreover, a detailed description of the term "hapten" is also contained in the specification as filed. For example, the specification describes the term "hapten" as including "an

immunological reactive molecule having a molecular mass of 100 – 2000 Da" (e.g., page 7, line 33 to page 8, line 1), "immunologically reactive peptide epitopes preferably having a length of up to 30 amino acids" (e.g., page 8, lines 21-22), "nucleic acids with a length of preferably up to 50 nucleotides that are complementary to a nucleic acid sequence which is to be detected in a sample," (e.g. page 8, lines 30-33), and "peptidic nucleic acids with a length of up to 50 monomeric units" (e.g., page 8, lines 33-35). Furthermore, numerous examples of specific haptens suitable for use in accordance with the claimed invention are provided on page 8 of the specification.

Similarly, it would have been well understood by one of ordinary skill in the art that the phrase "marker group" refers to a detectable moiety or label. A discussion of a related phrase, "luminescence label," excerpted from a review article by A. Mayer and S. Neuenhofer (*Angewadte Chemie international Edition in English*, 1994, *33*, pp. 1044-1072) is attached herewith as Exhibit B (in particular, see pages 1046 ff. and page 1054). Moreover, a detailed description of the phrase "marker group" may also be found in the specification as filed. For example, the specification describes the phrase "marker group" as including "luminescent metal chelates" (e.g., page 9, lines 3-4) and "fluorescent labels" (e.g., page 9, lines 3-4), numerous specific examples of which are provided on pages 9-11 of the specification.

In addition, it would have been well understood by one of ordinary skill in the art that the phrase "solid phase binding group" refers to any group through which an attachment can be made to a solid support (e.g., via chemical bond formation, etc). A discussion of solid phase binding groups is provided in the Mayer and Neuenhofer reference cited above (pages 1065 ff.). Moreover, representative examples of solid phase binding groups suitable for use in accordance with the present invention have been identified in the specification (e.g., page 9, lines 5-8) for purposes of illustration. These include biotin and biotin analogues such as desthiobiotin and iminobiotin.

Furthermore, it would have been well understood by one of ordinary skill in the art that the phrase "reactive side groups" refers to any functional groups (e.g., on the carrier) that can react with functional groups of complementary reactivity (e.g., on the haptens, marker groups, or solid phase binding groups) in order to form a bond. Representative examples of reactive side groups suitable for use in accordance with the

present invention have been identified in the specification (e.g., page 9, lines 10-16) for purposes of illustration. These include amino and thiol groups.

Likewise, it would have been well understood by one of ordinary skill in the art that the phrase "predetermined positions" refers to locations on the carrier containing a functional group available for reaction with a hapten, marker group, or solid phase binding group, or to the locations of the haptens, marker groups, or solid phase binding groups themselves. The specific positions will be determined on a case-by-case basis according to the specific requirements of an application. A detailed description of predetermined positions is set forth in the specification (e.g., page 6, lines 5-27).

Moreover, the phrase "non-immunologically reactive" is described in the specification (e.g., page 16, lines 3-8), and would be well understood by one of ordinary skill in the art as referring to amino acid sequences that "[do] not interfere with the test procedure in the intended application of the conjugate as an antigen in an immunological method of detection." One of ordinary skill in the art will recognize that the degree of non-reactivity required to meet this criterion may vary on a case-by-case basis according to the specific nature of the species to be detected and in accordance with well-established principles.

The recitation of a "polymeric carrier" containing nucleotides as monomeric units is fully supported by the description in the specification, and would be well understood by one of ordinary skill in the art. For example, the specification describes a representative structure for polymeric carriers composed of peptidic nucleic acids (e.g., page 7, lines 7-23), and identifies a reference (WO 92/20703) to provide additional instruction relating to petidic nucleic acids and their production (e.g., page 7, lines 21-23).

Finally, the recitation in claim 85 that the "polymeric carrier has a helical structure" is fully supported by the description in the specification, and would be well understood by one of ordinary skill in the art. As described in the specification, helical carriers include "single-stranded or double-stranded nucleic acids" (e.g., page 6, lines 21-27), and single-stranded or double-stranded peptidic nucleic acids (e.g., page 7, lines 25-29). Nucleic acids such as DNA are well known in the art, and it would be readily apparent to one of ordinary skill that nucleic acid backbones contain functionality

that can serve as points of attachment for haptens, marker groups, or solid phase binding groups.

Inasmuch as all terminology recited in the claims is both described in the specification and would be well understood by those of ordinary skill in the art, Applicants respectfully submit that the claims reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112, First Paragraph – Enablement

The enablement rejection of claims 72, 74-77, 80-81, 83-88, 100-101, and 106 under 35 U.S.C. § 112, first paragraph is respectfully traversed. The specification as filed provides one of ordinary skill in the art the wherewithal to practice the invention commensurate in scope with the present claims.

In accordance with MPEP 2164.08, "[h]ow a teaching is set forth, by specific example or broad terminology, is not important." *In re Marzocchi*, 439 F.2d 220, 223-224, 169 USPQ 367, 370 (CCPA 1971). While specific examples of polymeric carriers have been set forth in the specification, Applicants also provide direction and guidance of a more general nature to enable one of ordinary skill in the art to make and use alternative polymeric carriers. For example, oligonucleotide carriers and polymeric carriers composed of peptidic nucleic acids are described (e.g., page 7, lines 3-29), and a reference (WO 92/20703) is cited in order to provide additional instruction relating to petidic nucleic acids and their production (e.g., page 7, lines 21-23).

Similarly, while specific reactive groups have been identified in the specification, Applicants also provide direction and guidance of a more general nature to enable one of ordinary skill in the art to make and use alternative reactive groups. For example, as described in the specification, a desired reactive group can be introduced into the carrier chain by incorporating into the carrier a monomeric unit containing the reactive group (e.g., page 9, lines 10-16). Thus, for the purpose of illustration, the amino acids lysine, ornithine, hydroxylsine and cysteine are identified as "appropriate monomers" for

introducing reactive side groups such as amino side groups into the carrier chain (e.g., page 9, lines 14-16).

Likewise, while specific polymeric carriers have been described for use in accordance with the claimed invention, Applicants provide direction and guidance of a general nature to enable one of ordinary skill in the art to make and use alternative polymeric carriers having a helical structure. For example, the specification describes the relationship between spatial orientation of marker groups and signal strength in relation to helical carriers, and notes that "[the] distances between marker groups are ... preferably 3-6 or/and 13-16 monomeric units in the case of helical carriers. In addition, for the purpose of illustrating a representative helical polymeric carrier, a double-stranded helical carrier having one peptidic nucleic acid strand and one DNA strand is described (e.g., page 7, lines 25-29).

For all of the reasons set forth above, Applicants respectfully submit that the claimed invention is fully enabled. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The rejection of claims 72, 77, 80, 85, 87, 100-101, 103, and 105-106 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention, is respectfully traversed. As outlined below, each of the phrases identified in paragraphs A-F in section 12 of the Office Action has been described in the specification and/or has a well-defined meaning within the art.

As noted above and in the Mayer and Neuenhofer reference, the phrase "solid phase binding groups" refers to groups that can react specifically with a binding partner on a reactive solid phase. Thus, this phrase describes a specific interaction between a solid phase binding group and a solid phase resin.

As further noted above, the phrase "reactive side groups" is well understood in the art and has been explained in the specification (e.g., page 9, lines 10-16). The phrase refers without limitation to groups suitable for coupling haptens, marker groups, and solid phase binding groups to the carrier chain, and includes moieties such as

amino and thiol side groups. As described in the specification, reactive primary amino side groups "can be produced by incorporating appropriate monomers e.g., amino acids such as lysine, ornithine, hydroxylysine or cysteine into the carrier chain" (page 9, lines 14-16).

Similarly, as noted above, the phrase "non-immunologically reactive" is described in the specification (e.g., page 16, lines 3-8), and would be well understood by one of ordinary skill in the art as referring to amino acid sequences that "[do] not interfere with the test procedure in the intended application of the conjugate as an antigen in an immunological method of detection."

Furthermore, as noted above, the recitation of a polymeric carrier having "a helical structure" would be well understood in the art as including "single-stranded or double-stranded nucleic acids" (e.g., page 6, lines 21-27), and single-stranded or double-stranded peptidic nucleic acids (e.g., page 7, lines 25-29). As with other polymeric carriers embodying features of the claimed invention, hapten molecules, marker groups, and solid phase binding groups can be introduced at various stages in the preparation of conjugates using, for example, one of variants (a) and (b) described in the specification (e.g., page 11, line 32 to page 16, line 1).

The phrase "pharmacologically active substances" used in reference to haptens would be well understood by one of ordinary skill in the art as referring to a substance eliciting a physiological response in an individual. One of ordinary skill in the art will recognize that the magnitude of the response may vary considerably depending on the specific nature of the substance as well as on the individual. Moreover, the specification provides an extensive list of substances that qualify as "pharmacologically active substances" in the sense of the claimed invention (e.g., page 8, lines 1- 18), to which one of ordinary skill in the art may turn as a reference.

The recitation that the reactive side groups coupling the hapten molecules and the reactive side groups coupling the marker groups or solid phase binding groups are "alike" would be understood by one of ordinary skill in the art as referring to groups having the same chemical structure. For example, in Example 3 of the specification (e.g., page 25, line 24 to page 26, line 21), the amino side groups of the lysine monomeric units may be regarded as "reactive side groups" that are "alike" in the sense

of the claimed invention, such that after reacting these groups with a metal chelate marker group and a hormonal hapten, "[the] methal chelate and hapten molecules [will be] in each case coupled to the peptide chain via the ε-amino side group of the lysines" (e.g., page 26, lines 12-14).

For at least all of the reasons set forth above, Applicants respectfully submit that the present claims are not indefinite. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 102

By way of introduction, the claimed invention relates to conjugates containing hapten molecules and marker groups or solid phase binding groups at specific predetermined positions in precisely defined stoichiometries. Each of independent claims 72, 100, 101, 103, 105, and 106 recites "reactive side groups at predetermined positions on the polymeric carrier" (emphasis added). As a result of these predetermined positions, homogeneous compositions of conjugates are provided, which enable reproducible testing results in immunological assays. In contrast to the claimed invention, conjugates that incorporate functional groups (e.g. markers) in statistically unspecific ways result in heterogeneous compositions, which fulfill particular stoichiometries only statistically (i.e., as opposed to in the form of single molecules).

Moreover, the claimed invention further relates to conjugates containing carriers that are non-immunologically reactive, which prevents the carriers from reacting during the course of assays, and prevents cleavage of the carriers by common enzymes (e.g., trypsin, chymotrypsin, V8-protease, etc.) in human fluids (e.g., serum, plasma, urine, etc.).

The rejection of claims 72, 74-77, 80-81, 83, 86-87, 101, 103, and 105-106 under 35 U.S.C. § 102(b) as being anticipated by *Bredehorst et al.* (Anal. Biochem., 1991) is respectfully traversed. *Bredehorst et al.* does not teach or suggest "non-immunologically reactive" polymeric carriers, as recited in independent claims 72, 103, 105, and 106 of the claimed invention, nor does it teach or suggest conjugates containing more than one (i.e., 2-10) hapten molecules, as recited in independent claim

100 of the claimed invention, nor does it teach or suggest that the reactive side groups coupling hapten molecules and the reactive side groups coupling marker groups or solid phase binding groups should be "alike," as recited in independent claim 101 of the claimed invention.

Bredehorst et al. describes conjugates in which the carrier backbone "consists of the 21 amino acid residues of the insulin A-chain molecule" (e.g., page 272, first column), a naturally occurring peptide. It is noted that the cysteine units in the backbone are modified along their side chains and are properly considered as natural alpha amino acids, whereas the artificial amino acids of the claimed invention relate to beta-amino acids, gamma-amino acids, and the like, in which the amino group is not attached to the C-atom directly linked to the carboxyl group of the acid, but rather to a C-atom located further away. Thus, as noted in the Amendment and Reply filed on February 15, 2001, this insulin-A chain would likely interfere with immunological tests performed on patients (e.g., diabetics) having anti-insulin antibodies. In contrast to the potentially immunologically reactive carrier described in *Bredehortst et al.*, the carriers of independent claims 72, 103, 105, and 106 of the claimed invention are "non-immunologically reactive." *Bredehortst et al.* contains no teaching or suggestion to modify the carriers described therein to be "non-immunologically reactive," as called for by these claims. Likewise, *Bredehorst et al.* contains no teaching or suggestion to modify the carriers described therein to at least partially contain artificial amino acids, as further called for by independent claim 103.

Furthermore, *Bredehorst et al.* describes a conjugate "that provides a single site (terminal amino group) for attachment of [a single] hapten" (e.g., page 273, column 1; page 275, column 1). *Bredehorst et al.* contains no teaching or suggestion to modify the conjugates described therein to include more than a single hapten molecule, and no teaching or suggestion to include 2-10 hapten molecules as called for by independent claim 101.

In addition, *Bredehorst et al.* describes "trifunctional" conjugates in which the hapten molecule and the fluorophore are attached to the backbone of the carrier through different reactive groups (e.g., by a terminal amino group in the case of the hapten and by a carboxyl group in the case of the fluorophore; page 272, column 1).

Bredehorst et al. contains no teaching or suggestion that the reactive side group coupling hapten molecules and the reactive side groups coupling marker groups or solid phase binding groups be "alike," as called for by independent claim 101 of the claimed invention

Inasmuch as *Bredehorst et al.* fails to teach or suggest "non-immunologically reactive" polymeric carriers, the introduction of multiple hapten molecules into a polymeric carrier, and the use of one type of reactive group to attach each of a hapten and a marker group or a solid phase binding group, Applicants respectfully submit that the claimed invention is neither anticipated by nor would have been obvious in view of this reference. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of claims 72, 74-75, 77, 80-81, 83, 86-87, 100-101, 103, and 105-106 under 35 U.S.C. § 102(b) as being anticipated by *Buchardt et al.* (WO 92/2073) is respectfully traversed. *Buchardt et al.* does not teach or suggest a single conjugate containing 1-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claims 72, 101, 103, 105, and 106, nor does it teach or suggest a single conjugate containing 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claim 100 (emphases added).

Buchardt et al. does not teach or suggest the methods for forming conjugates described in the present application, whereby 1-10 monomeric units covalently bound to hapten molecules and an additional 1-10 monomeric units covalently bound to marker groups or solid phase binding groups (alternatively, monomeric units comprising protected reactive side groups) are introduced into the carrier at predetermined positions. As a result, the nucleic acid analogues described in *Buchardt et al.* will exhibit statistically controlled incorporation of hapten molecules and marker groups. Some of the nucleic acid analogues thus produced will contain haptens and/or marker

groups, while others will not. Moreover, two nucleic acid analogues contained in the same sample may exhibit different stoichiometries.

For at least these reasons, Applicants respectfully submit that the claimed invention is neither anticipated by nor would have been obvious in view of *Buchardt et al.* Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of claims 72, 74-75, 80, 86-88, 100, and 106 under 35 U.S.C. § 102(b) as being anticipated by *Tam* (US 5,229,490) is respectfully traversed. *Tam* does not teach or suggest a single conjugate containing 1-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claims 72, 101, 103, 105, and 106, nor does it teach or suggest a single conjugate containing 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claim 100 (emphases added).

The multiple antigen peptide systems described in *Tam* are principally directed to the production of vaccines based on peptide type antigens (e.g., col. 10, lines 27-29). *Tam* contains no teaching or suggestion of a carrier (e.g., a dendritic polymer) containing hapten molecules as well as marker groups or solid phase binding groups, as recited in the claimed invention. Indeed, even if the hydroxyl moiety of the first amino acid of the carrier were to be regarded as a solid phase binding group in the sense of the claimed invention, as suggested in the Office Action (i.e., page 17, last paragraph), then at least one element of the claimed invention—namely, that these species be coupled "to reactive side groups at predetermined positions on the polymeric carrier"— would still be lacking. The –OH group at the C-terminus of the peptide chain does not represent a free alcoholic hydroxyl group but, rather, the –OH is part of a carboxylic acid moiety –COOH. Moreover, this carboxylic acid moiety does not represent the only carboxylic acid moiety present on the peptide chain. Multiple carboxylic acid moieties are contained on the peptide chain (e.g., in the side chains of glutamate and aspartate residues), such that multiple equally reactive "solid phase binding groups" would be present, thereby resulting in binding of the carrier to a solid

phase at a variety of statistically determined (as opposed to predetermined and controlled) positions thereon.

For at least these reasons, Applicants respectfully submit that the claimed invention is neither anticipated by nor would have been obvious in view of *Tam*. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of claims 72, 74-76, 80, 86-88, 100, and 106 under 35 U.S.C. § 102(e) as being anticipated by *Rose et al.* (US 5,310,687) is respectfully traversed. *Rose et al.* does not teach or suggest a single conjugate containing 1-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claims 72, 101, 103, 105, and 106, nor does it teach or suggest a single conjugate containing 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups "coupled to reactive side groups at predetermined positions on the polymeric carrier," as called for by independent claim 100 (emphases added).

If the baseplate described in *Rose et al.* is regarded as a polymeric carrier in the sense of the claimed invention, and the so-called "complementary orthogonal specifically active molecules" (COSMs) attached thereto via oxime linkages are regarded as haptens in the sense of the claimed invention, then at least one element of the claimed invention—namely, a further 1-10 marker groups or 1-10 solid phase binding groups also attached to the baseplate via reactive side groups (e.g., oxime linkages)— would still be lacking. Moreover, if the hydroxyl moiety of the first amino acid of the carrier were, for the sake of argument, to be regarded as a solid phase binding group in the sense of the claimed invention, as suggested in the Office Action (i.e., page 19, last paragraph), such that the baseplate could be said to simultaneously contain 1-10 hapten molecules and 1-10 solid phase binding groups, then at least one element of the claimed invention—namely, that these species be coupled "to reactive side groups at predetermined positions on the polymeric carrier"— would still be lacking. As noted above, the –OH group at the C-terminus of the peptide chain does not represent a free alcoholic hydroxyl group but, rather, the –OH is part of a carboxylic acid moiety –COOH. Moreover, this carboxylic acid moiety does not represent the only

carboxylic acid moiety present on the peptide chain. Multiple carboxylic acid moieties are contained on the peptide chain (e.g., in the side chains of glutamate and aspartate residues), such that multiple equally reactive "solid phase binding groups" would be present, thereby resulting in binding of the carrier to a solid phase at a variety of statistically determined (as opposed to predetermined and controlled) positions thereon.

For at least these reasons, Applicants respectfully submit that the claimed invention is neither anticipated by nor would have been obvious in view of *Rose et al.* Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

The rejection of claims 72, 74-75, 80-81, 86-88, 100, 103-104, and 106 under 35 U.S.C. § 103(a) as being unpatentable over *Tam*, and the rejection of claims 72-76, 80-81, 86-88, 100, 103, and 106 under 35 U.S.C. § 103(a) as being unpatentable over *Rose et al.* are respectfully traversed for at least the reasons set forth above. Neither of *Tam* and *Rose et al.* teaches or suggests the entire combination of elements recited in the claimed invention. Accordingly, withdrawal of this ground of rejection is respectfully requested.

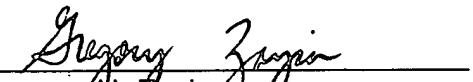
The rejection of claims 72-77, 80-81, 83, 84, 86-87, 101, 103, and 105-106 under 35 U.S.C. § 103(a) as being unpatentable over *Bredehorst et al.* in view of *Bard* (US 5,310,687) is respectfully traversed. As noted above, *Bredehorst et al.* does not teach or suggest (among other missing elements of the claimed invention) "non-immunologically reactive" polymeric carriers." Likewise, *Bard*, which describes luminescent metal chelate labels and means for detection, does not contain any teaching or suggestion of "non-immunologically reactive" polymeric carriers." Thus, inasmuch as the combination of *Bredehorst et al.* and *Bard* does not teach or suggest "non-immunologically reactive" polymeric carriers," Applicants respectfully submit that the claimed invention is neither anticipated by nor would have been obvious in view of *Rose et al.* Accordingly, withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of the Amendments and Remarks set forth above, Applicants respectfully submit that the claimed invention is in condition for allowance. Early notification to such effect is earnestly solicited.

If for any reason the Examiner feels that the above Amendments and Remarks do not put the claims in condition to be allowed, and that a discussion would be helpful, it is respectfully requested that the Examiner contact the undersigned agent directly at (312)-321-4257.

Respectfully submitted,



Gregory H. Zayia
Registration No. 48,059
Agent for Applicants

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200

COPY OF PAPERS
ORIGINALLY FILED

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments to paragraph beginning on page 5, line 25 and continuing to page 6, line 27:

"When using the conjugates according to the invention that contain 1 – 10 hapten molecules and a defined number of marker or solid phase binding groups as antigens in an immunological method of detection it is surprisingly possible to achieve [a considerable] considerably higher sensitivity and precision and at the same time [at] a reduced lower detection limit compared to known monomeric and multimeric antigens. Moreover the conjugates according to the invention can be constructed in a simple manner by solid phase synthesis e.g., a peptide solid phase synthesis. For [this] these monomeric units, e.g. amino acid derivatives, that are derivatized by a hapten molecule or a marker or solid phase binding group can be incorporated at predetermined positions. In addition it is possible to selectively incorporate additional haptens or marker or solid phase binding groups after completion of the solid phase synthesis at positions of the carrier chain at which monomers are located having free functional groups. This enables a defined and reproducible incorporation of hapten molecules and marker or solid phase binding groups into the conjugate. The distances between individual groups on the conjugate can be exactly defined and varied if necessary. The signal quenching can be kept low by selecting the distance of the marker groups on the conjugate so that the signal strength increases [proportionaly] proportionally to the number of marking groups. A defined spatial orientation of marker groups also contributes to the improvement of the signal strength e.g. in the case of helical carriers. The distances between marker groups are therefore preferably 3-6 or/and 13-16 monomeric units in the case of helical carriers e.g., single-stranded or double-stranded nucleic acids."